Clinical Trial Protocol
Iranian Registry of Clinical Trials

26 May 2026

Assessment of the Efficacy of High-Dose Intravenous Vitamin C on Severity of Acute Graft Versus Host Disease After Allogeneic Hematopoietic Stem Cell Transplantation: A Randomized, Triple-Blind, Placebo-Control Trial

Protocol summary

Study aim

Assessment of the Efficacy of High-Dose Vitamin C on Severity of Acute Graft Versus Host Disease After Allogeneic HSCT

Design

Prospective, Single-center, Triple-blind, Randomized, Placebo-Controlled Clinical Trial. The Balance Blocked Randomization method with Stata software will be used for randomization. The study will be conducted on 260 patients hospitalized in the bone marrow transplant departments of Shariati Hospital. After the number of patients reaches 28, an interim analysis will be done and based on that, a decision will be made regarding the continuation of the study.

Settings and conduct

Candidates for allogeneic transplantation of Research Institute of Oncology, Hematology and Cell Therapy are divided into two groups receiving vitamin C and placebo according to the random block list. Data are obtained by researchers in the BMT ward, post-transplant clinic, and emergency through questionnaires.

Participants/Inclusion and exclusion criteria

Inclusion criteria: Allogeneic HSCT due to hematologic malignancies; Patient age ≥ 18; HLA-full-matched stem cell related donor; normal kidney and liver function
Exclusion criteria: Known allergy to vitamin C; G6PDH deficiency; History of kidney stones or oxaluria during the last 5 years; Patients with hemochromatosis; Inability to swallow oral medicine from the 15th day onwards; Known or suspected state of malabsorption or gastrointestinal obstruction

Intervention groups

Vitamin C or placebo (50 mg/kg/day) is administered intravenously to each participant in 3 divided doses from day +1 after transplantation to day +14. Participants will then take vitamin C or a placebo in the form of oral effervescent 500 mg tablets once a day for up to 100 days after the transplant.

Main outcome variables

Cumulative incidence and severity of acute GVHD during 100 days after HSCT

General information

Reason for update

Acronym

VitCHSCT

IRCT registration information

IRCT registration number: **IRCT20140818018842N31**
Registration date: **2023-02-27, 1401/12/08**
Registration timing: **registered_while_recruiting**

Last update: **2023-02-27, 1401/12/08**
Update count: **0**

Registration date

2023-02-27, 1401/12/08

Registrant information

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Name of organization / entity

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date
2023-02-19, 1401/11/30
Expected recruitment end date
2023-09-21, 1402/06/30
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Assessment of the Efficacy of High-Dose Intravenous Vitamin C on Severity of Acute Graft Versus Host Disease After Allogeneic Hematopoietic Stem Cell Transplantation: A Randomized, Triple-Blind, Placebo-Control Trial

Public title
Vitamin C in Allogeneic Hematopoietic Stem Cell Transplantation
Purpose
Prevention
Inclusion/Exclusion criteria
Inclusion criteria:
Allogeneic hematopoietic stem cells transplantation due to any of the following hematological malignancies: Acute lymphoblastic leukemia (ALL)/ Acute myelogenous leukemia (AML)/ Myelodysplasia (MDS)/ Hodgkin's lymphoma (HL)/ non-Hodgkin's lymphoma (NHL) Patient age ≥ 18 Patients must also receive a full myeloablative conditioning regimen HLA-full-matched stem cell donor, either related or unrelated from peripheral blood stem cell or bone marrow Estimated creatinine clearance ≥60 ml/min Serum total bilirubin ≤ 2 x upper limit of normal value (ULN) and AST and ALT ≤ 2 x ULN Karnofsky Performance Status of 60-100% or Eastern Cooperative Oncology Group (ECOG) performance status ≤2 Ability to understand and the willingness to sign a written informed consent document
Exclusion criteria:
Known allergy to vitamin C G6PDH deficiency Patients with hemochromatosis History of kidney stones or oxaluria during the last 5 years Uncontrolled viral, fungal, or bacterial infection Allogeneic or autologous hematopoietic stem cells transplantation in the past 12 monthsPregnancy or breastfeeding Left ventricular ejection fraction < 40% Patient participation in another similar research project simultaneously Pregnancy or breastfeeding
Age
From **18 years** old
Gender
Both

Phase
2-3
Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

Sample size
Target sample size: **260**
Randomization (investigator's opinion)
Randomized
Randomization description
For randomization, the Balance Blocked Randomization method will be used Stata software. Random allocation will be done using blocks of sizes 6 and 8. The total sample size will be estimated as 260 patients. In this way, random samples will be determined using the ralloc module (Random allocation of treatments in controlled trials) in Stata software.
Blinding (investigator's opinion)
Triple blinded
Blinding description
Regarding the preparation of placebo: Injectable form: the treatment group will receive daily vitamin C in 5% dextrose and the control group will receive an equivalent volume of distilled water in 5% dextrose instead of vitamin C. Due to the blinding of the nursing staff, the preparation of the above solutions will be done by the pharmacist, who is not involved in the research but has the randomization list, in the clean room of the pharmacy of Shariati Hospital. Oral form: It is in the form of effervescent tablets of 500 mg, which drug and placebo with a completely similar appearance are prepared by a pharmaceutical company. The randomization sequence is prepared by a statistician who has no connection with the patients. The researchers and participants will be unaware of the study sequence. After confirming the entry of a new patient into the study and registering the patient's code, the coordinator who is stationed at the patient registration site places the patient in the treatment groups based on the specified randomization sequence.
Placebo
Used
Assignment
Parallel
Other design features
Since patient safety is the priority of this research, after the number of patients reaches 28, an interim analysis will be performed and a decision will be made regarding the continuation of the study.

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
The Institute of Pharmaceutical Sciences -Tehran University of Medical Sciences
Street address
Poursina St., Tehran University of Medical Sciences, Faculty Pharmacy, Institute of Pharmaceutical Sciences (TIPS)
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Province

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Approval date

2022-09-14, 1401/06/23

Ethics committee reference number

IR.TUMS.TIPS.REC.1401.049

Health conditions studied

1

Description of health condition studied

Allogeneic Hematopoietic Stem Cell Transplantation

ICD-10 code

Z94.84

ICD-10 code description

Stem cells transplant status

Primary outcomes

1

Description

Cumulative incidence and severity of acute GVHD

Timepoint

0 - 100 days after HSCT

Method of measurement

Patients will be monitored for acute GVHD at least daily until discharge and then at each outpatient visit until day 100+. The nature and extent of skin involvement will be determined by examination. Staging will be also based on the extent and type of skin involvement. Gastrointestinal GVHD requires 24-hour stool volume for staging. In addition, a history will be taken to document the presence or absence of abdominal pain, nausea, and vomiting. Patients will also be examined for the presence of ileus. The staging of liver involvement is also determined by the increase in total serum bilirubin. The grade of acute GVHD used to evaluate treatment will be the highest grade developed during the entire evaluation period.

Secondary outcomes

1

Description

Time from transplant to neutrophil engraftment

Timepoint

0 - 30 Days after HSCT

Method of measurement

Daily CBC or bone marrow aspiration and biopsy if needed

2

Description

Time from transplant to platelet engraftment

Timepoint

0 - 30 Days after HSCT

Method of measurement

Daily CBC or bone marrow aspiration and biopsy if needed

3

Description

Cumulative incidence, severity and duration of oral mucositis

Timepoint

0 - 100 days after HSCT

Method of measurement

Clinical assessment, oral and pharyngeal mucositis is evaluated clinically and based on CTCAE v5.0 daily until discharge or recovery and then at every outpatient visit to the clinic until day 100+.

4

Description

Safety and tolerability of the vitamin C regimen

Timepoint

0 - 100 days after HSCT

Method of measurement

Clinical assessment, Vitamin C adverse events (AEs) reported using criteria in the CTCAE v5.0

5

Description

Ascorbic acid plasma levels in patients receiving MAC regimen

Timepoint

0 - 30 days after HSCT

Method of measurement

With High-performance liquid chromatography (HPLC) method

6

Description

Relapse rates

Timepoint

At least 100 days after HSCT

Method of measurement

Bone marrow aspiration and biopsy.

7

Description

Overall survival

Timepoint

At least 100 days after HSCT

Method of measurement

Patient follow-up

Intervention groups

1

Description

Intervention group: IV vitamin C 50 mg/kg/day divided in

3 doses beginning on posttransplant; Day +1 and continuing through Day +14 Each dose of 1 g given in 100 mL of 5% dextrose/water over 30 minutes (33 mg/min) every 8 hours.After completion of the IV vitamin C doses, oral vitamin C 500 mg daily beginning on Day +15 and continuing until Day +100

Category
Treatment - Drugs

2

Description
Control group: Placebo IV Day +1 to +14, followed with oral, one placebo tablet daily beginning on Day +15 and continuing until Day +100.

Category
Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center
Research Institute of Oncology, Hematology, and Cell Therapy

Full name of responsible person
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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
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Full name of responsible person
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Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?
Yes

Title of funding source
Research Institute for Oncology, Hematology and Cell Therapy

Proportion provided by this source
100

Public or private sector
Public

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin

Type of organization providing the funding
Academic

Person responsible for general inquiries

Contact

Name of organization / entity
Tehran University of Medical Sciences

Full name of responsible person
Shima Heidari

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Resident of Pharmacotherapy

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Person responsible for updating data

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
No - There is not a plan to make this available
Justification/reason for indecision/not sharing IPD
There is no further information.
Study Protocol
No - There is not a plan to make this available
Statistical Analysis Plan
No - There is not a plan to make this available
Informed Consent Form
No - There is not a plan to make this available
Clinical Study Report
No - There is not a plan to make this available
Analytic Code
No - There is not a plan to make this available
Data Dictionary
Undecided - It is not yet known if there will be a plan to make this available